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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 07/15/2003

28

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

09/153,133

Applicant(s)

LEE ET AL.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/5/03.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 45-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 45-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 24.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Amendment filed on May 05, 2003 has been entered. Claims 45-60 are pending. Applicant is informed that the numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 46-61 been renumbered 45-60.

Priority

Priority of the instant application as set forth in Paper No. 6 is September 15, 1998.

Response to Amendment

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection that is not addressed in this Office Action is considered obviated in view of the amendment and arguments.

Double Patenting

Claims 45-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,214,368. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compositions

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comprising amorphous calcium phosphate for in vivo use. Accordingly, the scope of the claims overlap.

In the instant case, the patented claims are directed to formable paste composition comprising at least 90% calcium phosphate material and a second calcium phosphate material (see claim 45). The instant claims differ in the amounts of the amorphous calcium phosphate contained within the composition. However, modification of amounts can be achieved by routine experimentation, and the ordinary skill in the art would have had a reasonable expectation to observe beneficial clinical effects of calcium phosphate when administered in vivo.

Claims 45-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,117,456 and claims 1-12 of U.S. Patent 5,683,461. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compositions comprising amorphous calcium phosphate for in vivo use. Further both sets of claims only vary in amounts of calcium phosphate concentrations within the claimed compositions. However, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize such amounts by routine experimentations. Accordingly, the scope of the claims overlap and thus are obvious variants of each other.

Claim Rejections - 35 USC § 102

Claims 45-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Constantz US Patent 5,782,971 (Constantz).

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive because they are not directed to the scope of the pending claims.

The instant claims are directed to injectable paste compositions **comprising** a first adjuvant consisting essentially of amorphous calcium phosphate particles and a liquid component wherein the injectable paste composition has a solid content of greater than or equal to 40wt%. Contrary to applicant's interpretation of claims, the scope of pending claims is not directed to compositions consisting essentially of amorphous calcium phosphate. Rather, they are directed to compositions **comprising** a first adjuvant **consisting essentially of** amorphous calcium phosphate. Accordingly, the instant claims do not exclude the existence of other sources of calcium phosphate in the instantly claimed injectable paste composition.

Constantz on the other hand meets all elements of the instant claims. Constantz disclose injectable paste compositions comprising amorphous calcium phosphate mixtures in combination with a second calcium source such a hydroxyapatite, tetra calcium phosphate in amounts higher than 40 wt% (see abstract, col 4, lines 1-60; col 5, lines 1-10; claims 1-2, 16). The calcium phosphate containing compositions moieties of Constantz are flowable and injectable and are able to be combined with various organic compounds, proteins, growth factor etc.. which are encompassed by generic terms such as antigens, hapten, allergen or immunogens (see col 5, lines 60-66; col 6, lines 34-45, line 60-63). Thus, Constantz anticipates the limitations of the instant claims.

Further, as indicated in previous Office Action, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. *In re Casey*, 152 USPQ 235 (CCPA 1967). In the instant case, Constantz meets all elements of the instant claims and thus capable of performing the instant intended use and functional characteristics set forth in claims 51-53.

Finally, Applicant's arguments are elementally flawed. The instant claim 50 (previously 51) acquiesce to the fact that instantly claimed compositions of claims 45 and 46 (previously 46-47) comprise a secondary adjuvant such as hydroxyapatite (see instant claim 50). Constantz discloses the use of an additional calcium source such as hydroxyapatite (see claims 1-2, 16). Therefore, Constantz anticipates the scope of the pending claims.

Claims 45-56 are rejected under 35 U.S.C. 102(e) as being anticipated by Poser et al US Patent 5,968,253 (Poser).

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive. Similar to the arguments above Applicant's interpretation of the scope of the claims are not consistent with the presented arguments.

Further, Poser meets all elements of the instant claims. Poser at col 3, lines 47 discloses the use of tricalcium phosphate particles and amorphous calcium phosphate as suitable calcium phosphates. In addition, Poser discloses the use of penicillins and cephalosporins with his compositions. Such therapeutic agents are well recognized as

classic haptens, allergens or immunogens. Therefore, Poser's teachings anticipates the limitations of the instant claims.

Claim Rejections - 35 USC § 103

Claims 45-58 are rejected under 35 U.S.C. C. 103(a) as being unpatentable over Reyveld US Patent 4, 016,252, in view of Amerongen et al US Patent 5,443,832 and Constantz et al US Patent 5,782,971.

Applicant's arguments have been fully considered but are not found persuasive.

First, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the combined teachings of all references meet all the limitations of the instant claims. Therefore, the rejection is proper.

With respect to Applicant's position over Amerongen, Examiner again replies that Amerongen merely is used to show the effectiveness of hydroxyappetite in eliciting an immune response when it is administered in combination with an antigen. As applicant has correctly shown, the effectiveness of hydroxyappatite as an immune response eliciting agent is well evident in concentrations of as low as 0.499wt%. Therefore, the ordinary skill in the art would have had a reasonable expectation to observe similar capability at higher concentrations. Moreover, Constantz shows that higher concentrations hydroxyappattie is safe in the body. Therefore, the teachings of Constantz indicate that higher concentrations of hydroxyappatite to about 15 wt% of the

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dry ingredient (solid component) having particle sizes of about 0.5- 100 microns (col 5 lines 1-3; and lines 14-25). Constantz further indicates that one of ordinary skill in the art would be able to modify the viscosity of his composition by varying the percentages of solids in his composition, thus allowing for ease of administration (col 6, lines 32-39). Constantz also teaches that such composition can carry a suitable protein and be used as a drug delivery system (see col 5, lines 61-65 and col 6, line 62).

The Examiner has maintained the position throughout the history of the prosecution that one of ordinary skill in the art at the time of invention would have modified the concentrations of Relyveld calcium phosphate adjuvant composition to contain about 40 wt % solid component by routine experimentation and further formulate a hardenable calcium phosphate formulation, per teachings of Amerongen and Constantz, because even at higher concentration of solid components, such compositions are easily administered to the site of interest to elicit their intended clinical effects.

Furthermore, Applicant has not shown any unexpected results directed to the scope of pending claims. If calcium phosphate is taught by Relyveld or Amerongen to elicit an immune response at lower concentrations, it flows logically that such compound can also elicit an immune response at higher concentrations and one of ordinary skill in the art would have been able to ascertain such amounts by routine experimentations.

Finally, Applicant's arguments disregard the general knowledge available in the art. The central theme of Applicant's arguments is that calcium phosphate is not taught in the cited references in amounts of 40% wt and that the cited references do not teach

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injectable past formulations of calcium phosphate containing compositions. This line of arguments as pointed out in throughout the prosecution history are not persuasive, because, "the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In the instant case, one of ordinary skill in the art would have had a reasonable expectation of success when using higher concentrations of calcium phosphate in vivo at higher concentrations. Moreover, injectable paste is well taught by Constantz. Therefore, combining the cited references to make an adjuvant compositions or a hardenable bone cement would have been obvious because employing calcium phosphate compositions in said fields of endeavor is well established. Accordingly, the rejection is hereby maintained.

Claims 45-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Relyveld US Patent 4, 016,252, in view of Amerongen et al US Patent 5,443,832 and Constantz et al US Patent 5,782,971, as applied to claims 45-58 above, and further in view of and Gupta et al (Vaccine Design, Chapter 8 pp 229-248, 1995), or Kossovsky et al US Patent 5,462,751.

Applicant's arguments have been fully considered but are not found persuasive. Applicant argues that the primary and secondary references do not meet the limitations of the composition claims. However, Examiner rebutted such conclusion as argued above. Gupta and Kossovsky further teach that calcium phosphate products are used in

vaccine formulations and thus capable of eliciting an immune response. Therefore, the claims stand rejected.

Conclusion

No claims are allowed.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on October 28, 2002 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's Acting Supervisor, Padmanabhan Sreenivasan, can be reached on 703-305-1877. The

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fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.



RUSSELL TRAVERS
PRIMARY EXAMINER